UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,603	11/24/2003	Ananda M. Chakrabarty	51282-00013	6398

23767 7590 11/24/2006

PRESTON GATES ELLIS & ROUVELAS MEEDS LLP
1735 NEW YORK AVENUE, NW, SUITE 500
WASHINGTON, DC 20006

EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/720,603	CHAKRABARTY ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *11-19 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/28/04, 3/2/05, 7/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of group I in the reply filed on 9/15/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election of species melanoma is also acknowledged. Applicants point out that cupredoxin in claim 1 is inseparable from cupredoxin in claim 3 and request rejoining the nonelected inventions when the generic claim 1 is allowable. According to MPEP § 809.02(a):

> Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Additional species will be rejoined for examination if the generic claim is allowable based on MPEP 809.

After review and reconsideration of the elected species in light of the prior art, azurin as a species of cupredoxin is joined to the species of plastocyanin for examination at this time. Thus, claim 1-21 are pending. Claims 11-19 and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Claims 1-10 and 20 to the extent of azurin, plastocyanin and melanoma are examined on merits.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

This application claims benefit of U.S. provisional application No. 60/414550, filed on 8/15/03, which is acknowledged. The application claims benefit (CIP) of US non-provisional application No. 10/047710, which is also acknowledged. Upon review of specification of the application, 10/047710, it is noted that the application does not provide a support for the method of treating a condition to resistance to cell death in human melanoma cells comprising administering cupredoxin or plastocyanin, which binds

to p53. Therefore, for the purposes of examining this application, the examiner has established the effective priority dated of August 15, 2003, as the filing dated of the instant application for the claims 1, 2, 9 and 10 using cupredoxin or plastocyanin. If applicant disagree with any rejection set forth in this office action based on this priority date, applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 1/28/04, 3/27/05, 7/27/05, are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Claim Rejections - 35 USC § 112

The following is a quotation of the **second paragraph** of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-10 and 20 are indefinite because the term "an effective amount" in claim 1 is not clear. MPEP2173.05 state:

> *The phrase "an effective amount" has been held to be indefinite when the claim fails to state the function which is to be achieved and more than one effect can be implied from the specification or the relevant art. In re Fredericksen 213 F.2d 547, 102 USPQ 35 (CCPA 1954).*

The specification does not indicated what " an effective amount " is. The specification, although provide a teaching for treating a disease condition or a cell with variant amounts of azurin, does not teach what the effective amount is in the method. For example, figure 12-b show 100ug/ml wild type (wt) azurin has cytotoxicity to more than 50% of the cells, while in figure 14, the same amount of wt azurin has only 20% of cytotoxicity to the cells. Thus, one skilled in the art could not determine what "an effective

amount" is. Therefore, the metes and bounds of "an effective amount" in claim 1 cannot be determined, Claim 1 renders the dependent claims indefinite.

The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Drawn to written description

Claims 1-10 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of treating a condition related to resistant to cell death comprising administering an effective amount of a cupredoxin comprising azurin and plastocyanin, variant or derivative thereof to promote cell death, wherein the cupredoxin binds to p53. The claims further recite the azurin comprising the amino acid SEQ ID NO: 1 or at least 90% identity to SEQ ID NO: 1 and plastocyanin comprising amino acid SEQ ID NO: 2 or at least 90% identity to SEQ ID NO: 2. Thus, the claims are including using a genus of variants, derivatives of azurin and plastocyanin to treat a condition related to resistant to cell death.

The specification teaches a method of inducing breast cancer cell death by wild type azurin and plastocyanin (examples 21-22 and 23). The specification teaches an animal model established with melanoma tumors, which is treated with azurin (figure 6 and 8). The specification also describes mutants of azurin with a few amino acid substitutions (figure 11) and the their cytotoxicity to macrophage (figure 12). However, the specification does not teach **1)** a method of treating resistant cells with mutants or variants of plastocyanin comprising the polypeptide at least 90% identity to SEQ ID NO: 2; **2)** a method of administering any plastocyanin comprising mutants or any mutants of variants of azurin having at least 90% identity to SEQ ID NO: 1 to a subject with melanoma tumor; **3)** either plastocyanin or azurin or their mutants or variants binds to p53 in the process of inducing cell death or cytotoxicity.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristic, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613".

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d ,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information in the claimed method of treating a disease condition with variants, derivatives of azurin and plastocyanin. The specification does not provide a specific or detail structural characteristics of the variants or derivatives having 90% identity to azurin or plastocyanin of SEQ ID NO:1 or 2 used in the method. Thus, one of skill in the art would reasonably conclude that the inventor(s), at the time the application was filed, **did not have** possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above,

the skilled artisan cannot envision the detailed chemical structure(s) and functional attribute(s) of the encompassed genus of variants or derivatives of azurin and plastocyanin used in the method, and therefore conception is not achieved until **reduction to practice has occurred**, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a method of treating a condition related to resistance to cell death comprising administering azurin consisting of SEQ ID NO: 1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Drawn to enablement:

Claims 1-10 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands,* 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

The claims are broadly drawn to a method of treating a condition related to resistant to cell death comprising administering an effective amount of a cupredoxin comprising azurin and plastocyanin, variant or derivative thereof to promote cell death, wherein the cupredoxin binds to p53. The claims further recite the azurin comprising the amino acid SEQ ID NO: 1 or at least 90% identity to SEQ ID NO:1 and plastocyanin comprising amino acid SEQ ID NO: 2 or at least 90% identity to SEQ ID NO: 2.

The specification teaches a method of inducing breast cancer cell death by wild type azurin and plastocyanin (examples 21-22 and 23). The specification teaches an animal model established with melanoma tumors, which is treated with azurin (figure 6 and 8). The specification also describes mutants of azurin with a few amino acid substitutions (figure 11) and the their cytotoxicity to macrophage (figure 12). However, the specification does not teach **1)** a method of treating resistant cells with mutants or variants of plastocyanin comprising the polypeptide at least 90% identity to SEQ ID NO: 2; **2)** a method of administering any plastocyanin comprising mutants or any mutants of variants of azurin having at least 90% identity to SEQ ID NO: 1 to a subject with melanoma tumor; **3)** either plastocyanin or azurin or their mutants or variants binds to p53 in the process of inducing cell death or cytotoxicity. In addition, the specification on page 50-51, example 20-21 and figure 12-13, teaches that the mutants of azurin, M44KM64E (SEQ ID NO: 7), C112D (SEQ ID NO: 6), or S3S5 etc. do not have cytotoxicity to the cells and no apoptosis induction with these mutants, which does teach away from the claimed method of treating cell to promote cell death by administering the mutants or variants of azurin or plastocyanin. Thus, the specification fails to provide objective evidence, which enable the claimed method of treating a condition related to resistant to cell death comprising administering a variant or derivative of azurin or plastocyanin. The specification also fails to provide objective evidence, which azurin or plastocyanin or variants, derivative binds to p53 to promote the cell death.

It is well known in the art that proteins are folded 3-dimensional structures, the function and stability of which are directly related to a specific conformation (Mathews and Van Holde, Biochemistry, 1996, pp. 165-171). It is also know in the art that even a single modification or substitution in a protein sequence can alter the protein function. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic

fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al, Journal of Cell biology, Vol 111, p2129-2138, 1990). Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin (Schwartz et al., Proc Natl Acad Sci USA, vol 84, p6408-6411, 1987). Removal of the amino terminal histidine of glucagons substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase (Lin et al Biochemistry USA, vol 14, p1559-1563, 1975). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein.

The claims are broadly drawn to a method of treating a condition related to resistant to cell death comprising administering an effective amount of a azurin and plastocyanin, or variant or derivative thereof comprising amino acid having at least 90% identity to SEQ ID NO: 1 or 2. Since the specification does not provide claimed method as discussed above, one skilled in the art would not know how to use the claimed method on the basis of teachings in the prior art or instant specification.

In view of the lack of guidance, lack of examples, and lack of predictability associated claimed method of treating a condition related with cell death by administering azurin, or plastocyanin, or variant, or derivative thereof to promote cell death in a cell, one skilled in the art would be forced into under experimentation in order to practice the broadly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-6 are rejected under 35 U.S.C. 102(a) as being anticipated by Zaborina et al., (Microbiology, vol 146, page 2521-2530, Oct. 2000).

Claims are drawn to a method of treating a condition related to resistant to cell death comprising administering an effective amount of a cupredoxin comprising azurin to promote cell death, wherein the cupredoxin binds to p53. Since the claims do not specify administering to a subject or to cells, for the purpose of examination, the claims are interpreted as administering to a cell to promote cell death.

Zaborina et al., disclose a method of treating a condition related to resistant to cell death by contacting the resistant cell with effective amount of azurin in Q-sepharose column fraction. Zaborina et al., first teach that resistant cells in a condition of resistant to death (abstract) and then teach that the cells are induced to apoptosis by azurin assaying by LDH release (page 2526-2528, figure 5-8). Although Zaborina et al., do not explicitly teach azurin binding to p53, in the method, Zaborina et al., use the same material and the same cell population, and have the same active method steps. The Office treats the preamble language of the instant base claim as non-limiting, since the language does not result in manipulative difference in steps of claims. It is the Office's position that claimed method of treating a condition related to resistance to cells death by azurin to promote cell death is anticipated by Zaborina et al., because Zaborina et al., teaches the active step of instant method with the same material used for the same function, i.e. method of contacting death resistant cells with azurin, which would inherently result in binding p53 in the process of promoting cell death.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double-patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is either anticipated by, or would have been obvious over,

the reference claim(s). See, e.g. In reBerg, 140 F.3d, 1428, 46 USPQ2d 1226 (Fed. Cir. 1998): In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993): In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Claims 1,3, and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18, 20, and 21 of copending Application No.11435592 (592') and 19-22 of copending Application No.11488693 (693'). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1, 3, and 20 of instant application are drawn to a method of treating a condition related to resistant to cell death comprising administering an effective amount of a cupredoxin, or variant or derivative thereof, wherein resistance to cell death is human melanoma.

Claims 18 and 20-21 of 592' are drawn to a method of treating patient suffering cancer comprising administering to a patient with a therapeutically effective amount of a cupredoxin, wherein cancer is melanoma.

Claims 19-22 of 693' are drawn to method of treating patient suffering angiogenesis comprising administering to a patient with a therapeutically effective amount of a cupredoxin, wherein suffering is melanoma.

The claims in the instant application and claims in applications of 592' and 693' are directed to a method of treating patient suffering melanoma related disease comprising administering to a patient with a therapeutically effective amount of a cupredoxin. The only difference among the claim sets is cancer related disease is resistant to cell death in the instant application, cancer in the 592' and angiogenesis in the 693', which all are related with cancer comprising melanoma development and occurring.

It would have been *prima facie* obvious at the time the claimed invention was made to use the method to treat the melanoma with cupredoxin. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to use the method to treat a patient with melanoma because application 592' has shown a method of treating patient suffering cancer comprising administering to a patient with a therapeutically effective amount of a cupredoxin, wherein cancer is melanoma and because application 693' has shown method of treating patient suffering angiogenesis

comprising administering to a patient with a therapeutically effective amount of a cupredoxin, wherein suffering is melanoma.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Conclusion

No claims are allowed.

Claims 9-10 and 20 are free of art. As discussed in the rejection above, Zaborina et al., (Microbiology, vol 146, page 2521-2530, Oct. 2000) disclose a method of treating a condition related to resistant to cell death by contacting the resistant cell with effective amount of azurin, a species of cupredoxin. Zaborina et al., do not teach or suggest the method of treating a condition related to resistance to cell death comprising melanoma or using Plastocyanin or its variants.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER